REMARKS

Claims 7 to 31 have been filed and the original claims 1 to 6, which were English translations of foreign claims that were not drafted according to U.S. Patent Office Rules, have been canceled.

Claims 7 to 31 include method-of-treatment claims 7 to 15; method of making a two-layer-bioadhesive-tablet claims 16 to 25 and two-layer bioadhesive tablet claims 26 to 31. The method-of-treatment claims 7 to 15 include independent method claim 7 for a method of providing a controlled time-release profile of testosterone from a mixture of testosterone and at least one testosterone ester having a carboxylic acid group selected to provide the predetermined testosterone concentration profile. Method of making the two-layer-bioadhesive-tablet claims 16 to 25 include independent claim 16. The two-layer bioadhesive tablet includes an active ingredient layer including the mixture and an adhesive layer including an adhesive polymer.

Applicants acknowledge that the simultaneous amendment has not been entered since it was in German, not English.

The abstract of the disclosure was objected to because it was in two paragraphs. The abstract has been amended to overcome this objection and so that it is based on the new main claim 16. Withdrawal of the objection to the abstract is respectfully requested.

The lengthy original title was objected to and has been replaced by a shorter title that better describes the invention as claimed in the above new claims. The new title is only about 150 characters in length. It is difficult to draft a title that is sufficiently descriptive of the claimed invention with seven words or less. Approval of the new title and withdrawal of the objection to the title is respectfully requested.

The specification has been corrected by adding a brief description of the drawing figures as well as standard section headings. Figure 3 clearly illustrates the invention as it is now being claimed. Figures 1 and 2 have not been labeled "prior art", even though they do not describe examples of the claimed invention. Although testosterone alone has been previously administered to elderly men by various routes, apparently it has not been buccally administered by means of a bioadhesive tablet to human subjects (Voorspiels administered it in this manner but to dogs, not men). Testosterone unadeconate has been administered by a sublingual route to men, but apparently not by in a buccal method of administration by means of a bioadhesive tablet.

New claims 7 to 31 do not include any multiple claim dependencies (hence additional claims have been provided). Withdrawal of the claim objections is thus requested.

Claims 1 to 6 were non-statutory "Use" claims. These claims have been canceled, obviating their rejection under 35 U.S.C. 101. The new claims 7 to 31 do not include "use" claims. All three sets of claims have basis in the specification as originally filed.

Antecedent basis of claim terms has been checked. Other claim wording has been reviewed. For the foregoing reasons it is respectfully submitted that new claims 7 to 31 should not be rejected for indefiniteness under 35 U.S.C. 112, second paragraph

Claims 1, 2 and 4 to 6 were rejected under 35 U.S.C. 102 (b) as anticipated by Voorspoels, et al (herein referred to as "Voorspoels").

Claim 3 was rejected under 35 U.S.C. 103 (a) as obvious from Voorspoels.

Voorspoels measured the testosterone blood level in dogs after administration of testosterone or an ester of testosterone, by means of a buccal bioadhesive tablet. Voorspoels found that administration of testosterone itself by buccal administration is much preferred to oral administration in a tablet, because buccal administration avoids metabolization of testosterone in the liver, which can reduce the level of testosterone by 98 %. The resulting testosterone concentration profiles in the plasma for administration of testosterone and various esters are shown in Fig. 2 and Fig. 3. The level obtained using testosterone itself in the tablet is at least 4 to 10 x greater than using any of the

esters.

Voorspoels does not disclose a method of controlling the concentration profiles of testosterone by controlling relative amounts of testosterone and various selected testosterone esters administered to a person, *preferably* via buccal administration by means of a bioadhesive tablet.

Voorspoels does not disclose administering mixtures of testosterone and at least one testosterone ester. Similarly Voorspoels does not disclose a buccal bioadhesive tablet containing such mixtures.

Note the ratio from canceled claim 3 appears in new claims 7, 16 & 26.

It is well established that each and every element of a claimed invention must be disclosed in a single prior art reference, in order for the claimed invention to be anticipated by that reference. For example, the Federal Circuit Court of Appeals has said:

> " 'For a prior art reference to anticipate in terms of 35 U.S.C. 102, every element of the claimed invention must be identically shown in a single reference'.. These elements must be arranged as in the claim under review, but this is not an 'ipsissimis verbis' test ***In re Bond***, 15 U.S.P.Q. 2nd 1566 (Fed. Cir. 1990).

Thus it is respectfully submitted that none of the new claims 7 to 31 should be rejected under 35 U.S.C. 102 (b) as anticipated by Voorspoels.

Furthermore Voorspoels also found that the levels of testosterone obtained by buccal absorption of testosterone itself were much higher than those obtained by absorption of the testosterone esters (see page 1231, last paragraph, right hand column). This would lead on skilled in the art away from using the testosterone esters, either alone or in combination, with other

ingredients in methods for treating PADAM patients.

It is well established that teaching that would lead one skilled in the art away from the claimed invention cannot be used to reject a claimed invention as obvious (see M.P.E.P. 2145. X). Also the Federal Circuit Court of Appeals has said:

> "In determining whether such a suggestion [of obviousness] can fairly be gleaned from the prior art, ..It is indeed pertinent that these references teach against the present invention. Evidence that supports, rather than negates, patentability must be fairly considered." ***In re Dow Chemical Co.,*** 837 F.2nd 469,473, 5 U.S.P.Q.2d 1529, 1532 (Fed.Cir. 1988).

Voorspoels does not suggest the problem that one embodiment of the claimed method solves, namely matching the endogenous circadian rhythm of the testosterone blood level, as claimed in claim 9. A *prima facie* case of obviousness for the method of claim 9 is not established by this reference, because Voorspoels does not disclose or suggest this problem. See, for example, In re Nomiya, 184 USPQ 607,612 (C.C.P.A 1969); and Panduit Corp. v. Dennison Mfg. Co., 1 USPQ 2nd 1593,1600 (Fed. Cir., *cert. denied*, 481 U.S. 1052 (1987)).

Also the features of the method of dependent claims 8 and 17, namely selecting the testosterone ester or esters provided in the mixture according to chain length and steric structure, in order to provided the predetermined testosterone profile, are not suggested in Voorspoels. It is well established that the features of a claimed method must be suggested by any prior art reference used to reject the claimed method under 35 U.S.C. 103 (a). In the case of the

instant invention th features of claims 8 and 17 are not suggested by Voorspoels and thus this reference cannot be used to reject claims 8 and 17 under 35 U.S.C. 103 (a).

Also Voorspoels does not suggest the various adjuvants and auxillary ingredients.

For the foregoing reasons it is respectfully submitted that claims 7 to 31 should **not** be rejected under 35 U.S.C. 103 (a) as obvious over, or under 35 U.S.C. 102 (b) as anticipated by, Voorspoels.

APPENDIX SHOWING CHANGES MADE TO OBTAIN

THE AMENDED TITLE AND ABSTRACT

Underlining shows additions, brackets show deletions

In the Title:

The following changes were made:

BIOADHESIVE TABLET CONTAINING TESTOSTERONE/TESTOSTERONE ESTER MIXTURES AND METHOD FOR PRODUCING A PREDETERMINED TESTOSTERONE TIME-RELEASE PROFILE WITH SAME [Use of Testosterone Esters and/or Testosterone for Producing Buccally Applicable Bio-Adhesive Systems with Time-Released Active Ingredients]

In the Abstract:

Page 15, the following changes were made:

ABSTRACT OF THE DISCLOSURE

[The use of testosterone esters with 1 to 20 carbon atoms in the carboxylic acid radical or of mixtures of two or more testosterone esters with different carboxylic acid radicals and/or of testosterone, for producing buccally administered bioadhesive systems with time-controlled release of the active ingredient for the treatment of diseases associated with a modified testosterone level.

The use according to the invention makes it possible to attain in a tailored manner a therapeutic and/or circadian rhythm of the testosterone level.]

The method of making a bioadhesive tablet for controlling testosterone blood level, especially in elderly men suffering from partial androgen deficiency, includes spray-drying an alcoholic solution or suspension of testosterone and at least one testosterone ester, preferably in a ratio of 1:10 to 1:1.5, separately or together, with an organic polymer and optionally one or more auxiliary ingredient to form an active ingredient premix. Then various other auxiliary ingredients are mixed, as needed, with the active ingredient premix to form the bioadhesive tablet with an active ingredient layer and an adhesive layer. The active ingredient layer contains an effective amount of the active ingredient premix. The adhesive layer includes auxiliary ingredients including the bioadhesive polymer. The bioadhesive tablet may be buccally administered to provide a predetermined timed release profile of testosterone, advantageously varying according to a circadian rhythm.

Should the Examiner require or consider it advisable that the specification, claims and/or drawing be further amended or corrected in formal respects to put this case in condition for final allowance, then it is requested that such amendments or corrections be carried out by Examiner's Amendment and the case passed to issue. Any costs involved should be charged to the deposit account of the undersigned (No. 19-4675). Alternatively, should the Examiner feel that a personal discussion might be helpful in advancing the case to allowance, he or she is invited to telephone the undersigned at 1-631-549 4700.

In view of the foregoing, favorable allowance is respectfully solicited.

Respectfully submitted,

Michael J. Striker,

Attorney for the Applicants

Reg. No. 27,233